REMARKS/ARGUMENTS

Claims 9-11 and 14-29 are pending in the present application. Claims 1-8, 12 and 13 are canceled. Claims 19-29 have been withdrawn.

The Examiner has acknowledged that claim 18 is directed to patentable subject matter. Claims 13 and 14 are amended herein to change the word "homology" to "identity," which does not alter the scope of the claim, but merely conforms the language to that used in other claims herein. Claim 9 has been amended to correct nonsubstantive, typographical errors. New claim 30 is directed to an embodiment of the invention wherein the claimed enzyme has about 60% identity with SEQ ID NO. 8. Support for this claim is found in original claim 1.

Claims 9 and 14-17 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not provide an enabling disclosure of the claims.

Applicants respectfully disagree with the Examiner.

The Examiner maintains that the application is not enabling for enzymes having at least 75% homology to SEQ ID NO:8 and different from SEQ ID NO:8 in having an amino acid substitution at position 251, wherein the substituted amino acids are either Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly. In fact, the Examiner improperly indicates that to meet the enablement requirement of 35 U.S.C. § 112, first paragraph, the claimed enzyme must be encoded by either SEQ ID NO:1, 3 or 5.

In the Office Action the Examiner makes the following comments:

- *"Claims 9, 14-17 are so broad as to encompass any organophosphate degrading enzyme having at least 75% amino acid sequence identity to SEQ ID NO:8 and different from SEQ ID NO:8 in having a amino acid substitution at position 251, wherein the substituted amino acids are either Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly",*
- *"in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one said enzyme comprising the specific amino acid changes mentioned above",*

- *"The specification is limited to teaching the making and using amino acid sequence with SEQ ID NO:8 and differing from SEQ ID NO:8 in having an amino acid substitution at position 251, wherein the substituted amino acids are either Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly and wherein said polypeptide continues to having organophosphate hydrolysing activity but provides no guidance with regard to the making of variants and mutants as claimed or with regard to other uses",*

- *"the specification does not establish: (A) regions of the protein structure (except for the amino acid position 251) which may be modified without effecting activity",*

- *"specific guidance [is needed] regarding those amino acids that can indeed be modified without effecting the activity of the polypeptide", and*

- *"the specification does not establish: (A) regions of the protein (i.e. structure of SEQ ID NO:8) and polynucleotides (SEQ ID NO:7) which may be modified without effecting activity".*

Each of these statements is factually incorrect. As a preliminary matter, in the response to Office Action filed August 27, 2003, Applicants brought to the Examiner's attention the disclosure in the specification of the sequence of a protein other than SEQ ID NO:8 which is 75% identical to SEQ ID NO:8, which comprises an amino acid as defined at position 251, and possesses the defined activity (namely the *Musca domestica* protein provided as SEQ ID NO:13). Thus, the Examiner's statement concerning an alleged failure of the specification to provide guidance for making polypeptides within the scope of the claims is clearly inaccurate.

Applicants have provided considerable guidance regarding the regions of the protein structure which may be modified without effecting activity. In particular, the claims recite that conserved amino acids as shown in Figure 4 are maintained in the claimed enzyme and Applicants have shown that 25% of the amino acids in the non-conserved regions of the protein of SEQ ID NO:8 can be modified without effecting activity. Thus, the Examiner's statement that the specification does not establish which regions of the protein can be altered without affecting activity are unfounded.

The Examiner also states that "those skilled in the art need specific guidance regarding modifying specific amino acids that are not in the conserved region". It is respectfully submitted that such guidance has already been provided in the form of the protein alignments of the specification. Furthermore, it should be noted that the state of the art at the priority date with regard to the structure/function of esterases was well advanced. As support, the Examiner's attention is directed to a Rule 132 Declaration enclosed herewith executed by one of the inventors, Dr Robyn Russell. Further support can be found by reference to a review by Taylor and Radic (The Cholinesterases: from Genes to Proteins (1994) Annu. Rev. Pharmacol. Toxicol., 34:281-320); and two articles concerning the significant degree of sequence conservation between esterases across species in *Drosophila* (Evolutionary Genetics of Drosophila Esterases (1993) Genetica, 90:239-268; and Conservation and Change in Structure and 5' Flanking Sequences of Esterase 6 in Sibling Drosophila Species (1993) Genetica, 88:11-28), (copies enclosed). As a result, considering the information provided in the specification, and the advanced knowledge of esterase structure/function, it is submitted that more than sufficient guidance has been provided for one of ordinary skilled in the art to produce the molecules of the claimed invention.

It should also be noted that the inventors have a produced a molecule which is **63% identical** to that of the disclosed *L. cuprina* protein which maintains the activity of the claimed protein. More specifically, as outlined in the enclosed Rule 132 Declaration, a W251L mutant of the orthologous protein from *D. melanogaster* (the native protein was known at the priority date but the mutant was not) has been made and shown to possess the claimed activity. The mutant of the protein from *D. melanogaster* shares about 126 amino acids with the corresponding *L. cuprina* protein which **are not** found in the *M. domestica* protein (see Annexure B of the Dr

Russell's declaration). This means that there are a large number of proteins the skilled person could have readily produced at the priority date which possess the activity of the enzyme of new claim 30.

Furthermore, as outlined in the Rule 132 Declaration (see paragraph 6), the inventors have made yet a further molecule of the claimed invention which maintained the defined activity (see paragraph 6 of the declaration).

At page 6 of the Office Action the Examiner also asserts that

"without [such] guidance one or ordinary skill in the art would be reduced to the necessity of producing and testing all of the virtually infinite possibilities". This would clearly constitute undue experimentation".

It is difficult to comprehend the logic behind this statement. In actuality, there is no reason why the skilled person would bother performing the task suggested by the Examiner. The specification provides examples of proteins encompassed by the claims with the defined activity, and provides clear guidance with regard to amino acids which can be altered without effecting activity.

Considering the advance provided by Applicants' invention, it is unreasonable for the Examiner to limit the claims to only one of the specific molecule described in the specification. In particular, considering the guidance in the specification and the advanced knowledge of esterases in the art, one or ordinary skill in the art could readily arrive at a protein with one additional amino acid change (when compared to SEQ ID NO:8) which has the defined activity, but falls outside of the scope of the subject matter the Examiner believes is enabled by the present specification. An example of such an enzyme is provided in the Rule 132 Declaration provided herewith. As a result, the Examiner is implying that the subject matter of the claims should be unreasonably narrow, and hence would allow a third party to readily avoid

infringement. This would significantly reduce the value of the patent and not appropriately compensate the Applicants in light of the advance they have made.

In regards to the Examiner's assertion that the specification enables only enzymes having SEQ ID NO. 8 with an amino acid substitution at position 251 and encoded by SEQ ID NO. 1, 3, or 5, it is submitted that the Examiner has improperly applied this limitation. Recognizing that the state of the art has sufficiently developed to where an amino acid sequence might confer possession of the genus of encoding DNA sequences, the Federal Circuit in *In re Wallach*, (378 F.3d 1330, 71 U.S.P.Q.2d 1939 (Fed. Cir. Aug. 11, 2004) indicated that DNA molecules defined only in terms of the protein sequence, although containing a large number of species, are sufficiently definite to be deemed adequately described. The CAFC agreed with Appellants that a complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art may have been in possession of the entire genus of DNA sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious. The court also found no reason to require an applicant to list every possible permutation of nucleic acid sequences that can encode a particular protein for which the amino acid is disclosed since it is a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that encode it.

In the present case, the nucleotide sequence is not even being claimed, yet the Examiner asserts that the claimed protein whose complete amino acid sequence is provided is enabled only in terms of three specific nucleotide sequences. As noted by the CAFC, a complete polypeptide sequence is sufficient description of the genus of polynucleotide sequences capable of encoding

it, and therefore, the claimed sequence need not be defined by any particular nucleotide sequence that may encode it. Clearly, the Examiner's insistence on this limitation is improper.

It is respectfully submitted that the rejection of claims 9 and 14-17 under 35 U.S.C. § 112, first paragraph is respectfully traversed.

To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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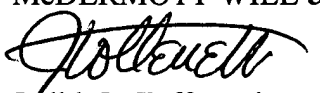

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